

We Claim:

1. A monoclonal antibody that specifically binds human ghrelin at an epitope localized to amino acids 4-20 of human ghrelin.
- 5 2. The antibody of Claim 1, wherein the ghrelin is acylated or unacylated.
3. A monoclonal antibody that specifically binds a peptide comprising amino acids 4-20 of human ghrelin.
- 10 4. The antibody of any one of Claims 1-3 comprising at least one peptide selected from peptides with a sequence selected from the group consisting of:
  - a) SEQ ID NO: 5, 6, 7, 20, 22 or 28 located at CDR1 of the light chain variable region (LCVR);
  - b) SEQ ID NO: 8 located at CDR2 of the LCVR;
  - c) SEQ ID NO: 9, 21, 23 or 29 located at CDR3 of the LCVR;
  - d) SEQ ID NO: 14, 15, 16 or 24 located at CDR1 of the heavy chain variable region (HCVR);
  - e) SEQ ID NO: 17, 25 or 26 located at CDR2 of the HCVR; and
  - f) SEQ ID NO: 18 or 27 located at CDR3 of the HCVR.
- 20 5. The antibody of any one of Claims 1-3 comprising at least two peptides selected from peptides with a sequence selected from the group consisting of:
  - a) SEQ ID NO: 5, 6, 7, 20, 22 or 28 located at CDR1 of the light chain variable region (LCVR);
  - b) SEQ ID NO: 8 located at CDR2 of the LCVR;
  - c) SEQ ID NO: 9, 21, 23 or 29 located at CDR3 of the LCVR;
  - d) SEQ ID NO: 14, 15, 16 or 24 located at CDR1 of the heavy chain variable region (HCVR);
  - e) SEQ ID NO: 17, 25 or 26 located at CDR2 of the HCVR; and
  - f) SEQ ID NO: 18 or 27 located at CDR3 of the HCVR.

-65-

6. The antibody of any one of Claims 1-3 comprising at least three peptides selected from peptides with a sequence selected from the group consisting of:
  - a) SEQ ID NO: 5, 6, 7, 20, 22 or 28 located at CDR1 of the light chain variable region (LCVR);
  - b) SEQ ID NO: 8 located at CDR2 of the LCVR;
  - c) SEQ ID NO: 9, 21, 23 or 29 located at CDR3 of the LCVR;
  - d) SEQ ID NO: 14, 15, 16 or 24 located at CDR1 of the heavy chain variable region (HCVR);
  - e) SEQ ID NO: 17, 25 or 26 located at CDR2 of the HCVR; and
  - f) SEQ ID NO: 18 or 27 located at CDR3 of the HCVR.
- 5  
10  
15  
20  
25  
30  
7. The antibody of any one of Claims 1-3 comprising at least four peptides selected from peptides with a sequence selected from the group consisting of:
  - a) SEQ ID NO: 5, 6, 7, 20, 22 or 28 located at CDR1 of the light chain variable region (LCVR);
  - b) SEQ ID NO: 8 located at CDR2 of the LCVR;
  - c) SEQ ID NO: 9, 21, 23 or 29 located at CDR3 of the LCVR;
  - d) SEQ ID NO: 14, 15, 16 or 24 located at CDR1 of the heavy chain variable region (HCVR);
  - e) SEQ ID NO: 17, 25 or 26 located at CDR2 of the HCVR; and
  - f) SEQ ID NO: 18 or 27 located at CDR3 of the HCVR.
8. The antibody of any one of Claims 1-3 comprising at least five peptides selected from peptides with a sequence selected from the group consisting of:
  - a) SEQ ID NO: 5, 6, 7, 20, 22 or 28 located at CDR1 of the light chain variable region (LCVR);
  - b) SEQ ID NO: 8 located at CDR2 of the LCVR;
  - c) SEQ ID NO: 9, 21, 23 or 29 located at CDR3 of the LCVR;
  - d) SEQ ID NO: 14, 15, 16 or 24 located at CDR1 of the heavy chain variable region (HCVR);
  - e) SEQ ID NO: 17, 25 or 26 located at CDR2 of the HCVR; and
  - f) SEQ ID NO: 18 or 27 located at CDR3 of the HCVR.

-66-

9. The antibody of any one of Claims 1-3, comprising peptides with the sequence shown in:

SEQ ID NO: 5, located at CDR1 of the LCVR;  
SEQ ID NO: 8, located at CDR2 of the LCVR;  
5 SEQ ID NO: 9, located at CDR3 of the LCVR;  
SEQ ID NO: 14, located at CDR1 of the HCVR;  
SEQ ID NO: 17, located at CDR2 of the HCVR; and  
SEQ ID NO: 18, located at CDR3 of the HCVR.

- 10 10. The antibody of any one of Claims 1-3, comprising peptides with the sequence shown in:

SEQ ID NO: 6, located at CDR1 of the LCVR;  
SEQ ID NO: 8, located at CDR2 of the LCVR;  
SEQ ID NO: 9, located at CDR3 of the LCVR;  
15 SEQ ID NO: 15, located at CDR1 of the HCVR;  
SEQ ID NO: 17, located at CDR2 of the HCVR; and  
SEQ ID NO: 18, located at CDR3 of the HCVR.

- 20 11. The antibody of any one of Claims 1-3, comprising peptides with the sequence shown in:

SEQ ID NO: 20, located at CDR1 of the LCVR;  
SEQ ID NO: 8, located at CDR2 of the LCVR;  
SEQ ID NO: 21, located at CDR3 of the LCVR;  
SEQ ID NO: 24, located at CDR1 of the HCVR;  
25 SEQ ID NO: 25, located at CDR2 of the HCVR; and  
SEQ ID NO: 27, located at CDR3 of the HCVR.

- 30 12. The antibody of any one of Claims 1-3, comprising peptides with the sequence shown in:

SEQ ID NO: 22, located at CDR1 of the LCVR;  
SEQ ID NO: 8, located at CDR2 of the LCVR;  
SEQ ID NO: 23, located at CDR3 of the LCVR;

-67-

SEQ ID NO: 24, located at CDR1 of the HCVR;  
SEQ ID NO: 26, located at CDR2 of the HCVR; and  
SEQ ID NO: 27, located at CDR3 of the HCVR.

- 5        13. The antibody of any one of Claims 1-3, wherein the LCVR comprises a peptide with the sequence shown in SEQ ID NO: 3, 4, 30 or 31.
- 10      14. The antibody of any one of Claims 1-3, wherein the HCVR comprises a peptide with the sequence shown in SEQ ID NO: 12, 13, 32 or 33.
- 15      15. The antibody of any one of Claims 1-14 which comprises a heavy chain constant region selected from the group consisting of IgG<sub>1</sub>, IgG<sub>2</sub>, IgG<sub>3</sub> or IgG<sub>4</sub>.
16. The antibody of any one of Claims 1-14 which comprises a kappa or lambda light chain constant region.
17. The antibody of any one of Claims 1-14 which is a Fab fragment.
18. The antibody of any one of Claims 1-14 which is a F(ab')<sub>2</sub> fragment.
- 20      19. The antibody of any one of Claims 1-14 which is a single chain Fv fragment.
- 25      20. The antibody of any one of Claims 1-14 wherein a CDR has 2 or 1 conservative amino acid substitutions or terminal deletions.
21. The antibody of any one of Claims 1-14 which is chimeric.
22. The antibody of any one of Claims 1-14 which is humanized.
- 30      23. The antibody of any one of Claims 1-22 which is labeled.

-68-

24. The antibody of Claim 23, wherein the label is selected from the group consisting of:

- (a) an enzyme label;
- (b) a radioisotope;
- 5 (c) a fluorescent label; and
- (d) biotin.

25. An isolated nucleic acid molecule that encodes an antibody of any one of Claims 1-14.

10

26. An expression vector comprising the nucleic acid molecule of Claim 25.

27. A host cell comprising the vector of Claim 26.

15

28. A method of synthesizing an anti-hGhrelin monoclonal antibody comprising culturing a host cell of Claim 27 such that an anti-hGhrelin monoclonal antibody is expressed in the cell and purifying the antibody from the cell or from the culture media in which said cell is grown.

20

29. A process of generating an anti-hGhrelin monoclonal antibody comprising,

- a) immunizing a non-human animal with a peptide comprising 8, 9, 10, 11, 12, 13, 14, 15, 16 or 17 contiguous amino acids of a peptide spanning amino acid residues 4-20 of human ghrelin in which 1, 2 or 3 of said contiguous amino acids are selected from amino acids 4, 5 and 6 of human ghrelin, and
- 25 b) isolating an antibody from the immunized animal which antibody specifically binds a peptide spanning amino acids 4-20 of both acylated hGhrelin and des-acyl hGhrelin.

30. A monoclonal antibody made by the process of Claim 29.

30

31. A chimeric antibody comprising the CDRs of an antibody of Claim 30.

-69-

32. A humanized antibody comprising the CDRs of an antibody of Claim 20.
33. A pharmaceutical composition comprising the antibody of any one of Claims 1-24, 30, 31 and 32.

5

34. The pharmaceutical composition of Claim 33 further comprising a pharmaceutically acceptable carrier.
35. The pharmaceutical composition of Claim 33 or Claim 34 wherein the antibody is the active ingredient.

10

36. A method of detecting the acylated and/or the des-acyl form human ghrelin in a biological sample comprising contacting the biological sample with the antibody of any one of Claims 1-3 and detecting the human ghrelin protein in the biological sample.

15

37. A method of treating or preventing obesity or a related disorder comprising administering to a human in need thereof a therapeutically effective amount of the pharmaceutical composition of any one of Claims 33-35.

20

38. The method of Claim 37 wherein the disorder is selected from the group consisting of obesity, NIDDM, Prader-Willi syndrome, eating disorders, hyperphagia, impaired satiety, anxiety, gastric motility disorders, cancer and cardiovascular disorders.

25

39. An article of manufacture comprising a packaging material and an antibody contained within said packaging material, wherein the antibody neutralizes ghrelin activity for treatment or prevention of a human suffering from a disorder in which ghrelin activity is detrimental, and wherein the packaging material comprises a package insert which indicates that the antibody neutralizes by binding human ghrelin.

30

-70-

40. The article of manufacture of Claim 39, wherein the antibody is the antibody of any one of Claims 1-24